

Remarks

Upon entry of the foregoing amendments, claims 1, 15-49, 54-56, 62, 63 and 65-73 are pending in the application, with claims 1, 16, 17, 49, 55, 56, 63 and 67 being the independent claims. Claim 73 is sought to be amended. Claims 2-14, 50-53, 60, 61, 64 and 57-59 were cancelled by previous amendment. Claims 1, 15, 49, 54-56, 62, 63, 65 and 66 were previously withdrawn from further consideration as being drawn to a non-elected invention, there allegedly being no allowable generic or linking claim.

Based on the following remarks, Applicants respectfully request that the Office reconsider all outstanding rejections and objections and that they be withdrawn.

Claim Objection

Claim 73 was objected to because the term "heterarylene" was misspelled. (Office Action, at page 2.) Claim 73 has been amended to correct the spelling of "heterarylene." Accordingly, Applicants respectfully request that this objection be withdrawn.

Double Patenting Rejection

Claims 16-48 and 67-73 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1, 4-27, 29 and 37 of U.S. Pat. No. 7,173,102 B2 ("the '102 patent"). (Office Action, at page 3.)

Specifically, the Examiner contends that although the allegedly conflicting claims are not identical, "they are not patentably distinct from each other because a method of killing microorganisms by contacting a surface with a compound of formula II is disclosed." (*Id.*) Additionally, the Examiner states "[t]he specific embodiments of

formula II as well as the motivation to administer to an animal in need of treatment for a microbial infection are discussed below [for the reasons claims 16-48 and 67-73 are rejected under 35 U.S.C. § 103(a)]." (*Id.*)

Applicants respectfully traverse the Examiner's rejection of claims 16-48 and 67-73 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4-27, 29 and 37 of the '102 patent for at least the following reasons.

Applicants respectfully submit the Examiner improperly relied upon the underlying disclosure of the '102 patent for motivation to perform the methods of claims 16-48 and 67-73 of the current application in the Examiner's analysis. As described in more detail below, the Examiner pointed only to disclosures in the written description of the '102 patent as providing motivation for performing the methods of claims 16-48 and 67-73 of the current application and not to the claims of the '102 patent. According to The Manual of Patent Examining Procedure, a "double patenting rejection of the obviousness-type, if not based on an anticipation rationale, is 'analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. 103' except that the patent principally underlying the double patenting rejection is not considered prior art." MPEP § 804(I)(B)(1) (2007)(alterations in original). Because the disclosure of the '102 patent is not considered prior art, Applicants respectfully submit the Examiner improperly relied upon the disclosure in the patent underlying the double patenting rejection for providing motivation to perform the methods of claims 16-48 and 67-73 of the current application. Accordingly, for at least this reason, Applicants respectfully request the Examiner withdraw the rejection of claims 16-48 and 67-73 under the judicially created

doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4-27, 29 and 37 of the '102 patent.

Additionally, claims 16-48 and 67-73 of the current application are directed to a method of treating a microbial infection in an animal, the method comprising administering to the animal an effective amount of a pharmaceutical composition comprising an amphiphilic oligomer of Formula II and a pharmaceutically acceptable carrier or diluent. Thus, the claims are directed to pharmaceutical uses of the disclosed oligomers, *i.e.*, to methods of treating a microbial infection in which a pharmaceutical composition of one of the oligomers is administered to an animal, *e.g.*, administered parenterally as a solution to the animal to treat the microbial infection.

In contrast, claims 1 and 4-25 of the '102 patent are directed to a polymer or oligomer of a specific formula. Additionally, claims 26 and 27 of the '102 patent are directed to a method of killing microorganisms, the method comprising the steps of providing a substrate having disposed thereon a contact-killing, facially amphiphilic polymer or oligomer or claim 1, claim 14 or claim 20 and placing the polymer or oligomer disposed thereon on the substrate in contact with a microorganism to allow formation of pore in the cell wall of the microorganism. Claim 29 of the '102 patent is directed to a microbiocidal composition comprising a facially amphiphilic polymer or oligomer of claim 1, claim 14, or claim 20 and a solid support, *e.g.*, wood, synthetic polymers, natural and synthetic fibers, cloth, paper rubber and glass. Claim 37 of the '102 patent is directed to an antimicrobial composition comprising a facially amphiphilic polymer or oligomer of claim 1, claim 14, or claim 20 and a composition selected from

the group consisting of paint, coatings, lacquer, varnish, caulk, grout, adhesives, resins, films, cosmetics, soap and detergent.

As described in more detail below, Applicants submit that, contrary to the Examiner's statements, claims 16-48 and 67-73 of the current application would not have been obvious in light of claims 1, 4-27, 29 and 37 of the '102 patent, because a person of ordinary skill in the art, in light of the '102 patent, would not have had a reason to administer a pharmaceutical composition of a polymer to be applied to the surface of or incorporated into an object and a pharmaceutically acceptable carrier to treat an animal with a microbial infection.

Applicants believe the rejection of 16-48 and 67-73 under the judicially created doctrine of obviousness-type double patenting has been overcome and respectfully request that the Examiner reconsider and withdraw the rejection.

Rejection Under 35 U.S.C. § 103(a)

Claims 16-48 and 67-73 are rejected under 35 U.S.C. § 103(a) as being allegedly obvious over DeGrado *et al.* U.S. Pat. No. 7,713,102 ("the '102 patent"). Applicants respectfully traverse this rejection.

Applicants submit that the Examiner's rejection of claims 16-48 and 67-73 of the current application is improper under 35 U.S.C. § 103(c)(1). 35 U.S.C. § 103(c)(1) recites

[s]ubject matter developed by another person, which qualifies as prior art only under one or more of subsections (e), (f), and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the

claimed invention was made, owned by the same person or subject to an obligation of assignment to the same person.

35 U.S.C. § 103(c)(1). The '102 patent qualifies as prior art to the current application under only 35 U.S.C. § 102(e). At the time the invention of the current application was made, one or more of the inventors was subject to an obligation of assignment to the same entity as the '102 patent. Assignments from the inventors of both the '102 patent and the current application to the Trustees of the University of Pennsylvania have been recorded with the PTO. The assignments from the inventors of the '102 patent were recorded with the PTO on December 16, 2004, and may be found at Reel 015461, Frame 0418, while the assignments from the inventors of the current application were recorded with the PTO on December 30, 2004, and may be found at Reel 015502, Frame 0019. Therefore, Applicants respectfully submit the Examiner's rejection of claims 16-48 and 67-73 of the current application under 35 U.S.C. § 103(a) is improper.

However, Applicants herein address the Examiner's rejection of the claims under 35 U.S.C. § 103(a) as being obvious on the merits.

The Examiner asserts the claimed invention is obvious because

[i]t would have been prima facie [sic] obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to administer to an animal infected with a microorganism a pharmaceutical composition comprising a compound of formula I or II as disclosed by [the '102 patent].

A person of ordinary skill in the art would have been motivated to administer to an animal infected with a microorganism a pharmaceutical composition comprising an oligomer of formula I or II because: (1) [the '102 patent] give[s] the general teaching that the disclosed oligomers inhibit the growth of microorganisms; (2) [the '102 patent]

teach[es] that testing of the bacterial efficacy of the disclosed oligomers have been performed in mammals; (3) [the '102 patent] teach[es] a need to design the disclosed oligomers with reduced toxicity to birds, fish, mammals, and other higher organisms; (4) [the '102 patent] teach[es] that any object that is exposed to or susceptible to bacterial or microbial contamination can be treated with the disclosed oligomers; and (5) [the '102 patent] give[s] the general teaching that both pets and agronomic animals are often exposed to and harbor a variety of infectious pathogenic organisms that can cause disease in animals or humans. Therefore, a person of ordinary skill in the art would have had a reasonable expectation of success in treating a microbial infection in an animal by administering a pharmaceutical composition comprising the preferred oligomers disclosed in [the '102 patent].

(*Id.* at pages 5-6.)

Initially, the Examiner stated a person of ordinary skill in the art would have been motivated to treat an animal with a microbial infection by administering a pharmaceutical composition comprising an oligomer of *Formula I or II*. (*Id.* at page 5)(italics added). However, claims 16-48 and 67-73 of the current application are directed to a method of treating a microbial infection in an animal comprising administering an effective amount of a pharmaceutical composition comprising an amphiphilic oligomer of *Formula II* and a pharmaceutically acceptable carrier or diluent. Previously withdrawn claims 1 and 15 are directed to a method of treating a microbial infection in an animal comprising administering an effective amount of a pharmaceutical comprising an amphiphilic oligomer of *Formula I* and a pharmaceutically acceptable carrier or diluent. Applicants respectfully wish the Examiner to clarify whether claims 1 and 15 are also currently being examined, in addition to claims 16-48 and 67-73.

Applicants submit the Examiner has taken the statements from the '102 patent out of context and is not considering the disclosure of the '102 patent as a whole. For

example, the Examiner states "[t]esting of the bacterial efficacy has been performed in mammals with these polymers in water (col. 24, lines 57-64, example 5-6)." (*Id.* at page 4.) However, col. 24, lines 57-59 of the '102 patent recite: "[t]o determine the toxicity to mammalian, as well to bacterial, *cells* the biocidal activity is evaluated using both cultured cells and freshly obtained human blood cells." (The '102 patent, col. 24, lines 57-59)(emphasis added). Additionally, Example 5 of the '102 patent describes an *in vitro* assay conducted to determine the antibacterial activity of the disclosed polymers and does not describe the bacterial efficacy of the polymers in a mammal. (*Id.*, at col. 32, lines 30-38.) Furthermore, Example 6 of the '102 patent describes an *in vitro* assay to be conducted to determine the toxicity of the disclosed polymers on mammalian cells, not a mammal. (*Id.*, at col. 32, lines 44-56.) Therefore, Applicants submit the toxicity of the polymers were tested in an *in vitro* assay, not *in vivo* in mammals as the Examiner asserts. As such, Applicants submit the '102 patent does not disclose that the polymers are safe to be administered to an animal, and a person of ordinary skill in the art would not have been motivated to administer these polymers to an animal with a microbial infection.

Additionally, the Examiner alleges the '102 patent "teaches a need to design these polymers with reduced toxicity to birds, fish, mammals, and other higher organisms." (The Office Action, at page 4.) However, the '102 patent states "[o]ne object of the invention is to provide new polymeric compounds with anti-microbial properties which can be applied to or dispersed throughout devices, articles and surfaces and which are capable of killing microorganisms on contact, but *leach* into the environment more slowly than traditional small molecule anti-microbials." (The '102 patent, at col. 4, lines

60-65)(emphasis added). Additionally, the '102 patent states "[f]acially amphiphilic molecules with molecular weights of about 0.8 kD to about 20 kD will be more prone to *leach* from the surface of the substrate." (*Id.*, at col. 5, lines 57-59.) Therefore, Applicants submit that, in context, the disclosure in the '102 patent regarding the polymers having reduced toxicity to birds, fish and mammals indicates the inventors' concern regarding the toxicity of the polymers after leaching from the surface of the object and does not suggest the polymers would be safe for administration to an animal with a microbial infection.

Furthermore, the Examiner alleges the '102 patent discloses that "[b]oth pets and agronomic animals are exposed to and harbor a variety of infectious pathogenic organisms that can cause disease in animals or humans (col. 27, lines 1-28.)" (Office Action, at page 4.) However, Applicants again respectfully submit that, in context, this statement would not motivate a person of ordinary skill in the art to administer the polymers disclosed in the '102 patent to treat an animal with a microbial infection. Specifically, the '102 patent discloses

[a]ny object that is exposed to or susceptible to bacterial or microbial contamination can be treated with these polymers. These needs are particularly acute in the health care and food industries. A growing concern with preservatives has produced a need for new materials that prevent microbiological contamination without including preservatives. The incidence of infection from food-borne pathogens is a continuing concern and antimicrobial packaging material, utensils and surfaces would be valuable. In the health care and medical device areas the utility of antimicrobial instruments, packaging and surfaces are obvious. Products used internally or externally in humans or animal health including, but not limited to, surgical gloves, implanted devices, sutures, catheters, dialysis membranes, water filters and implements, all can harbor and transmit pathogens. The polymers of the

present invention can be incorporated into spinnable fibers for use in materials susceptible to bacterial contamination including fabrics, surgical gowns, and carpets. Ophthalmic solutions and contact lenses easily become contaminated and cause ocular infections. Antimicrobial storage containers for contact lens and cleaning solutions would be very valuable. Both pets and agronomic animals are exposed to and harbor a variety of infectious pathogenic organisms that can cause disease in animals or humans.

(The '102 patent, at col. 27, lines 1-29.) Applicants respectfully submit that, in context, this paragraph suggests that pets and agronomic animals may spread infectious pathogenic organisms to untreated surfaces and does not suggest that the polymers should be administered to an animal with a microbial infection.

Contrary to the Examiner's assertion, claims 16-48 and 67-73 of the current application would not have been obvious in light of the '102 patent, for at least the following reasons. The '102 patent describes the use of antimicrobial polymers and oligomers attached to surfaces or incorporated into an object and retain their ability to act as an antimicrobial agent. A polymer or oligomer that functions as an antimicrobial agent, when attached to a surface, such as wood or cloth, or incorporated into an object, such as a catheter or contact lens, would not necessarily be expected to be effective in treating a microbial infection in an animal when administered to the animal, *e.g.*, by parenteral injection of a pharmaceutical composition, as recited by claims 16-48 and 67-73 of the current application.

Additionally, the '102 patent provides no guidance to a person of ordinary skill in the art as to what route the polymers could be administered to an animal or with which pharmaceutically acceptable carriers or diluents the polymers are compatible. Furthermore, the '102 patent does not provide any information as to how the polymers

are metabolized and whether any toxic metabolites are formed upon administration to the animals. Instead, the '102 patent provides ample guidance as to how to apply the polymers to the surface of an object, such as wood, paper, and plastic. (The '102 patent, at col. 27, line 29 through col. 29, line 2.) Additionally, the '102 patent provides guidance as to how to incorporate the polymers into an object, such as a catheter or paint. (*Id.*, at col. 29, lines 3-60.) Therefore, a person of ordinary skill in the art would not have been motivated to administer a pharmaceutical composition containing an oligomer of Formula II with a pharmaceutically acceptable carrier or diluent to an animal with a microbial infection, as recited in claims 16-48 and 67-73 of the current application in light of the '102 patent.

Furthermore, the '102 patent suggests to a person of ordinary skill in the art, when applying the disclosed polymers to the surface of an object, to use a polymer with a much higher molecular weight than an oligomer of Formula II with 1 to about 20 monomer units that is to be administered in the method of claims 16-48 and 67-73 of the current application. The '102 patent discloses the polymers or oligomers to be applied to the surface of an object include a number of monomer units of 2 to at least about 500. (The '102 patent, at col. 12, line 25.) However, the '102 patent also discloses "[f]acially amphiphilic molecules with molecular weights of about 0.8 kD to about 20 kD will be more prone to leach from the surface of the substrate." (*Id.*, at col. 5, lines 57-59.) Therefore, a person of ordinary skill in the art that is preparing a composition to be applied to the surface of an object would be motivated to use a polymer with a number of monomer units on the higher end of the disclosed range to prevent or reduce leaching of the polymer from the surface, rather than use a polymer with a number of monomer units

on the lower end of the disclosed range. As such, a person of ordinary skill in the art would not have been motivated to administer a pharmaceutical composition containing an oligomer of Formula II with a maximum number of monomer units of about 20 to an animal with a microbial infection, as recited in claims 16-48 and 67-73 of the current application, in light of the '102 patent.

Thus, the *in vivo* administration of a pharmaceutical composition containing an antimicrobial oligomer of Formula II with 1 to about 20 monomer units and a pharmaceutically acceptable diluent or carrier to treat an animal with a microbial infection, as recited by claims 16-48 and 67-73 of the current application, would not have been obvious in light of the *in vitro* use of the substrate-bound antimicrobial polymers as antimicrobial agents, as described in the '102 patent.

As evidence of the nonobviousness of claims 16-48 and 67-73 of the current application in light of the '102 patent, Applicants will provide submit as a Declaration under 37 C.F.R. § 1.132 of David P. Nicolau, Pharm.D., FCCP. Dr. Nicolau is an expert in the field of anti-infective agents.

As further evidence of the nonobviousness of claims 16-48 and 67-73 of the current application in light of the '102 patent, Applicants will provide a Declaration under 37 C.F.R. § 1.132 of Harry Bermudez, Ph.D. Dr. Bermudez has expertise in the field of biopolymers.

Conclusion

All of the stated grounds of rejection and objection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Marsha A. Rose

Marsha A. Rose
Attorney for Applicants
Registration No. 58,403

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1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600

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